

EXHIBIT I



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Important Product Safety Information

Kineret® is a medicine that is used to reduce the pain and swelling associated with moderate to severe active rheumatoid arthritis. Kineret® is a man-made protein that is similar to a naturally occurring protein called interleukin-1 receptor antagonist (IL-1ra) found in the body. Kineret® is for use by patients eighteen years of age or older and for patients who have not responded to treatment with other agents called disease-modifying antirheumatic drugs or DMARDs. Kineret® can be used by itself or in combination with DMARDs. Kineret® should not be used with medicines called Tumor Necrosis Factor (TNF) blocking agents such as ENBREL® (etanercept), Humira™ (adalimumab), or Remicade® (infliximab).

Kineret® has been associated with an increased incidence of serious infections (2%) vs. placebo (< 1%). Kineret® should be discontinued if a patient develops an infection, however most patients can continue taking Kineret® after their infection resolves. Kineret® should not be initiated in patients with active infections. Kineret® should not be used with TNF-blocking agents such as etanercept, adalimumab, and infliximab.

A 7% rate of serious infections was observed in a 24-week study of concurrent administration of Kineret® and etanercept.

Kineret® is contraindicated in patients with known hypersensitivity to *E coli*-derived proteins, Kineret®, or any components of the product.

Percent of RA Patients Reporting Adverse Events with a Frequency of ≥ 5% in Kineret®-treated Patients Over a 6-month Period in Clinical Trials

Preferred Term	Placebo (n = 733)	Kineret® 100 mg/day (n = 1565)
Injection-Site Reaction	29%	71%
Worsening of RA	29%	19%
URI	17%	14%
Headache	9%	12%
Nausea	7%	8%
Diarrhea	5%	7%
Sinusitis	7%	7%
Arthralgia	6%	6%
Flu-Like Symptoms	6%	6%
Abdominal Pain	5%	5%

Adverse events included those that were observed for patients in 2 clinical trials of Kineret® who received 100mg/day fixed dose. Patients in one study (N = 899) were on stable doses of methotrexate. Patients in the second study (N = 1399) included those who were on a variety of RA medications including some DMARD therapies and those who were DMARD-free.

The most common side effect of Kineret® in clinical trials was injection site reaction (ISR) which was usually mild, characterized by redness, swelling, and pain, and lasted for 14 to 28 days. The development

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of ISRs in patients who had not previously experienced them was uncommon after the first month of therapy.

View full Kineret® patient product information page.

**RHEUMATOID ARTHRITIS
KINERET® AND RHEUMATOID ARTHRITIS
DIET & EXERCISE
REIMBURSEMENT
IMPORTANT PRODUCT SAFETY INFORMATION**

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In clinical trials there was a risk of serious infections (2% in Kineret® patients vs. less than 1% in placebo patients). Kineret® should be discontinued if you develop an infection, however most often you can continue taking Kineret® after your infection resolves. You should not use Kineret® if you are taking TNF-blocking agents, such as etanercept, adalimumab, and infliximab, unless your doctor has told you to do so. If you use Kineret® with etanercept, adalimumab, or infliximab you may increase your risk of getting a serious infection. Kineret® should not be used if you know you are hypersensitive to *E. coli*-derived proteins, Kineret®, or any ingredient of the product. The most common side effect in clinical trials was a reaction at the site of injection, which was usually mild and characterized by redness, swelling, and pain.

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